

Please Stand By

You will hear silence until the presentation  
begins

The HIV/STD/TB/Hepatitis Program, Division of Disease Control, conducts Lunch and Learn Webinars for health-care professionals in North Dakota.

Each month a new topic will be held from 12:00 p.m. to 1:00 p.m. CST on the **fourth Wednesday of the month.**

Next month's L&L : January 27, 2016

Register: <http://www.ndhealth.gov/HIV/events.htm>

Please complete the post-test to receive CEU's for this presentation. You must score at least 70% to receive credit.

This presentation will be archived and available for later viewing on:

[www.ndhealth.gov/HIV/Resources/resources.htm](http://www.ndhealth.gov/HIV/Resources/resources.htm)

For questions or comments contact:

Gordana Cokrljic

701.328.2379

[gcokrljic@nd.gov](mailto:gcokrljic@nd.gov)

# Announcement

- The Association of Public Health Laboratories (APHL), in collaboration with Center for Disease Control and Prevention (CDC), is presenting an **Overview of Syphilis Diagnostics**.
  - Three-part series of free, short interactive web-based modules describing the common serologic methods used in the laboratory to diagnose a syphilis infection.
    - Background and History (15 minutes)
    - Serologic Assays and Algorithms (15 minutes) and
    - Case Studies (8 cases)
  - Link for the modules: <http://www.aphl.org/aphlprograms/infectious/std/Pages/STD-syphilis.aspx>
  - For questions contact Anne Gaynor at [anne.gaynor@aphl.org](mailto:anne.gaynor@aphl.org) or 240.485.2739.
  - A new document called **Suggested Language for Syphilis Serology Testing** will be published by Christmas.

# Syphilis

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## Lunch & Learn

**Sheila Lukehart, PhD**  
**Julie Dombrowski, MD**

**December 2015**

# Outline

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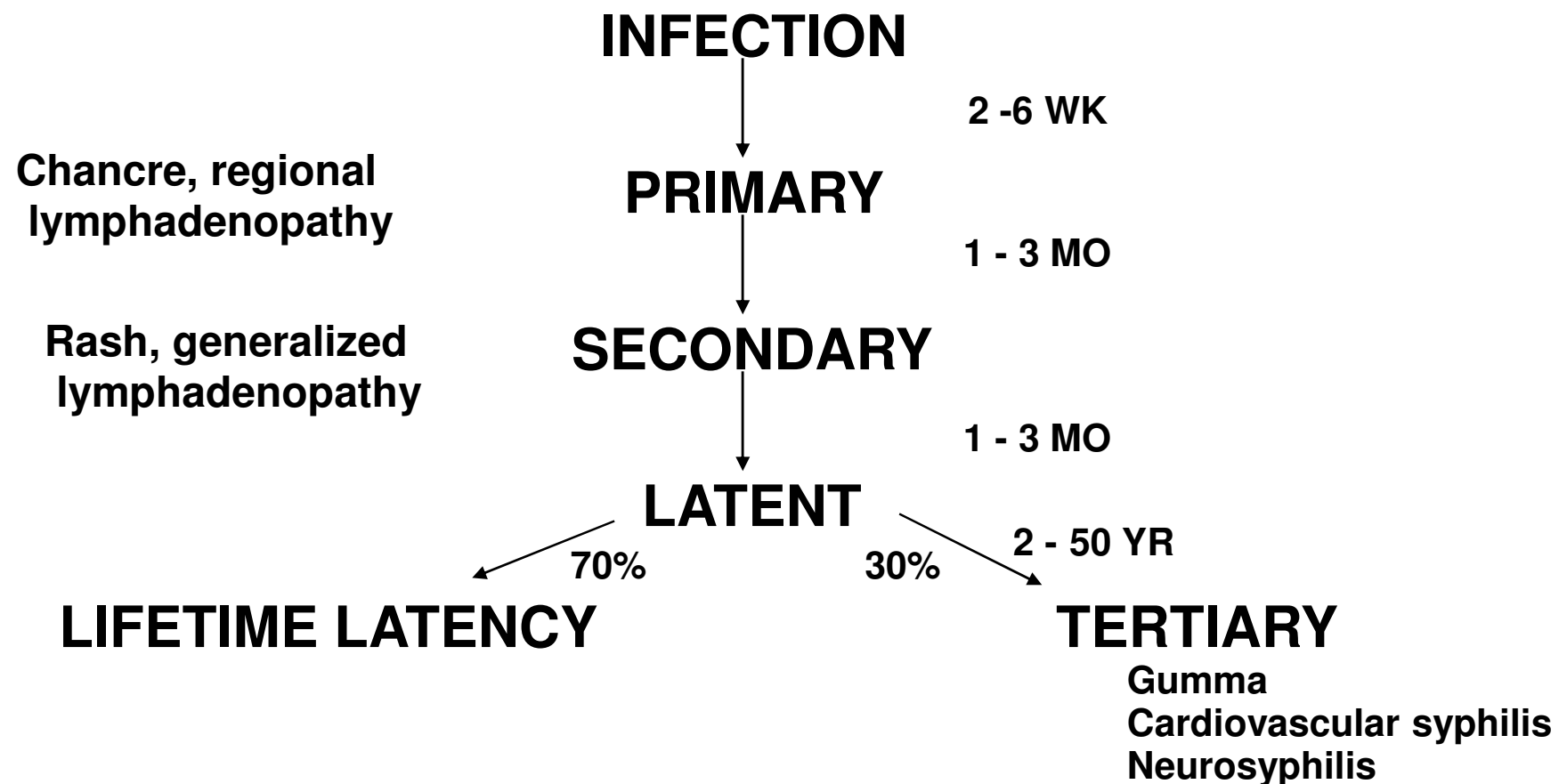
- Clinical manifestations
- Diagnostic tools
- Treatment and follow-up
  - Management in pregnant women
  - Management in HIV coinfection
- Management of sexual partners

# Syphilis

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- Chronic sexually transmitted infection caused by *Treponema pallidum*
- Characterized by episodes of active clinical disease interrupted by periods of subclinical (latent) infection
- Early manifestations involve primarily skin, mucosal surfaces; late manifestations may affect any organ system

# Natural History of Untreated Syphilis





# Epidemiology of Syphilis

## U.S. Current Trends

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- Cases of P&S increased 3 fold from 2000-2014
- 15% increase between 2013 and 2014
- Current major outbreaks are in MSM, 50-70% HIV+
- 23% increase in women from 2013-2014

# Epidemiology of Syphilis: U.S.

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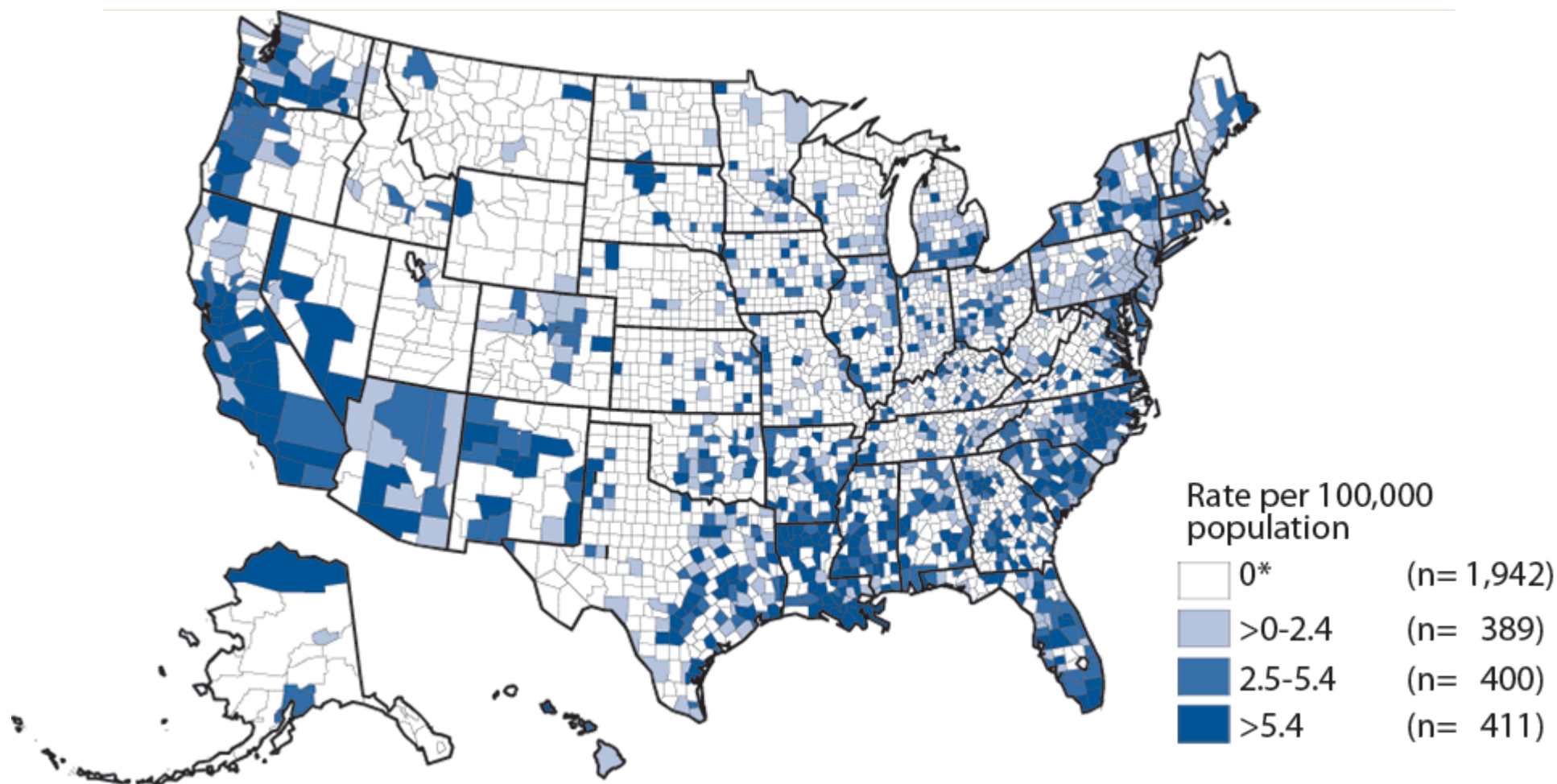
- 2014 cases

Primary, Secondary	19,999
All stages	63,450
Congenital	458*

**\*28% increase from 2013-2014**

Data from 2014 STD Surveillance, CDC

# Infectious Syphilis 2014– by County



STD Surveillance 2014, CDC

# Syphilis in North Dakota

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- 2014 cases

Primary, Secondary	13
All stages	51*
Congenital	0

**\*9-fold increase from 2010 to 2014**  
**2-fold overall increase from 2013-2014**

Data from 2014 STD Surveillance, CDC

# Etiology

- *Treponema pallidum* subsp. *pallidum*
  - Venereal syphilis
  - Corkscrew-shaped, microaerophilic, noncultivable
  - 10-14  $\mu\text{m}$  in length, 0.5  $\mu\text{m}$  in diameter



# Syphilis

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- Mode of Transmission
  - Direct contact with infectious lesion
- Incubation Period
  - 9-90 days, average is 2-6 weeks

# Primary Syphilis

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- Painless, indurated chancre: genital, anal, or oral
- Firm regional lymph nodes
- Lasts 1-5 weeks; heals spontaneously



# Primary Chancre--Male

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# Healing chancre

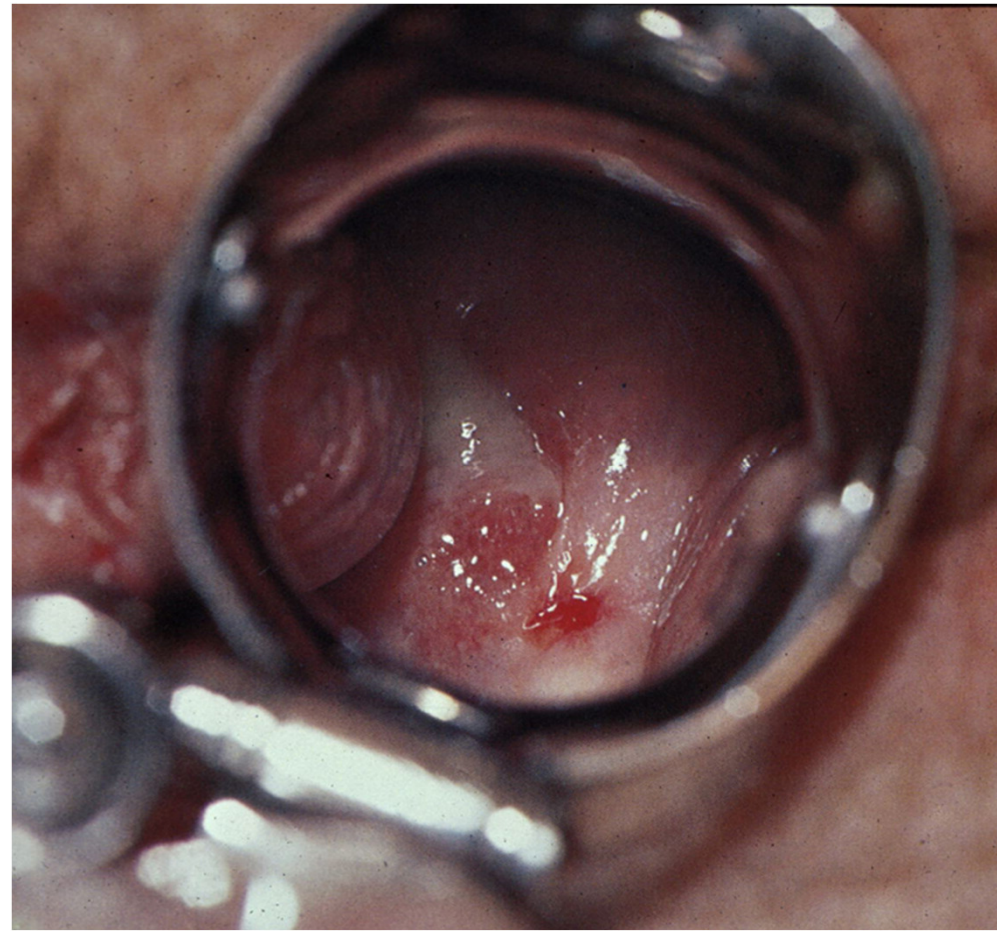
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# Chancre--Female

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# Chancre



# Secondary Syphilis

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- 15% have persisting/healing chancres
- Generalized rash: Macular, papular, pustular, or combination
- Generalized lymphadenopathy (88%)
- Mucous patches (10%)
- Condylomata lata (10%)

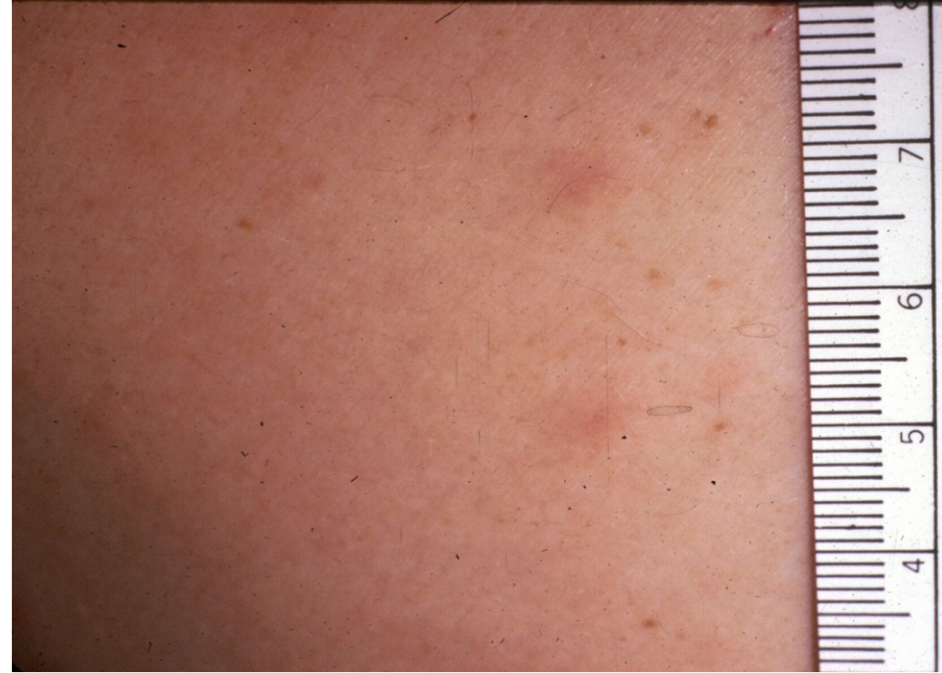
# Secondary Syphilis

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- Headache, fever, malaise
- Alopecia, liver or kidney involvement
- Lasts 2-6 weeks; resolves spontaneously
- 25% have recurrent secondary symptoms, within one year

# Macular syphilis

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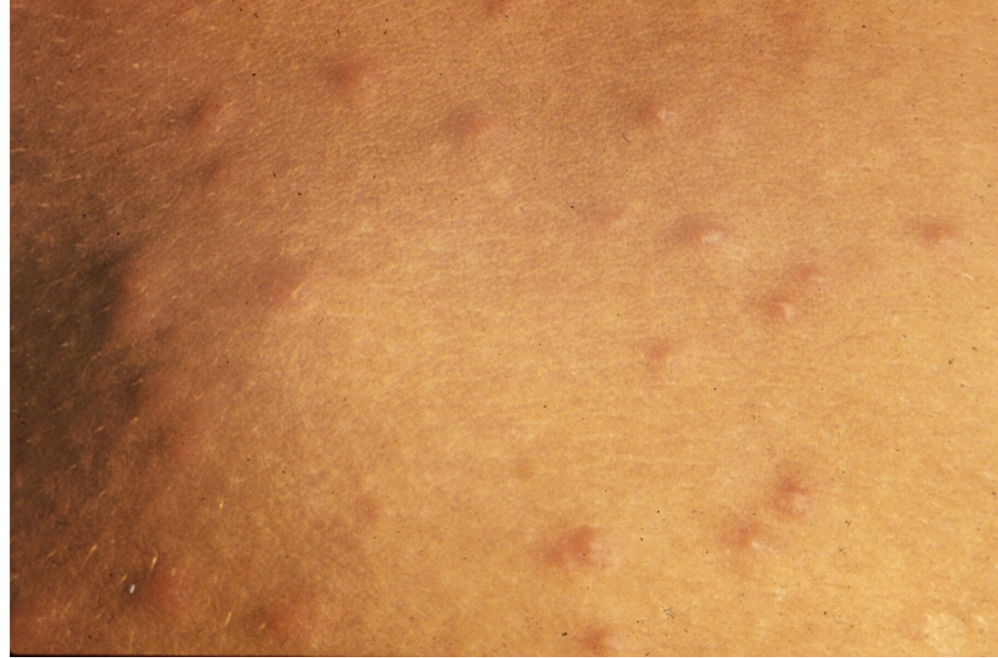


Closeup



# Papular Syphilis

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Closeup

# Secondary Syphilis—Palms & Soles





# Secondary Syphilis

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**Mucous Patches**



**Condylomata lata**

Begovac and Lukas  
N Engl J Med 2005; 352:708

# Latent Syphilis

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- No clinical manifestations
- Positive serologic tests for syphilis
- < 1 year – early latent
- > 1 year – late latent
- 2/3 of patients with untreated syphilis remain in latent stage for life

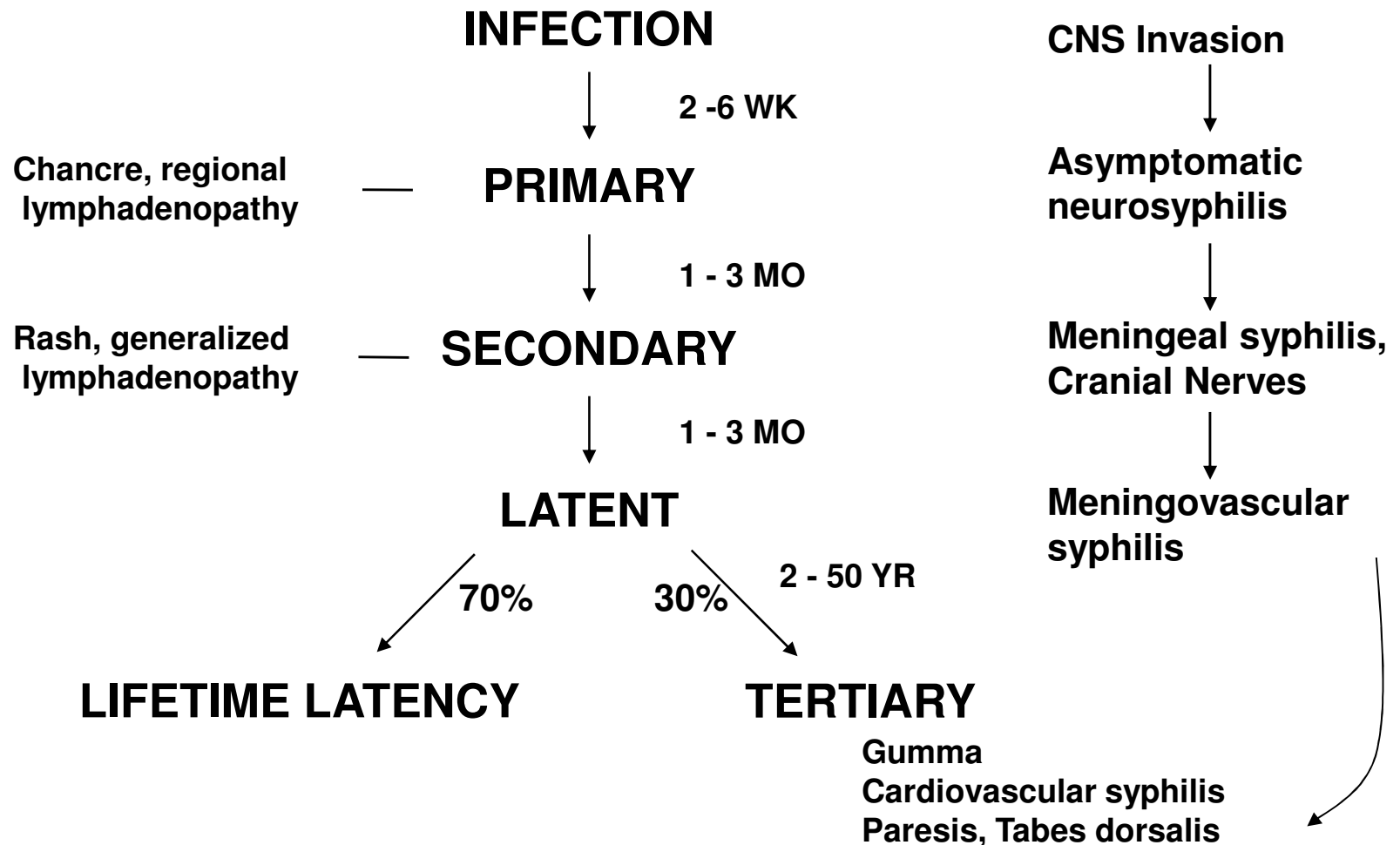
# Tertiary Syphilis

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- 33% of untreated patients (preantibiotic era)
  - Late benign (Gumma)
  - Cardiovascular
  - Paresis, Tabes Dorsalis



# Natural History of Untreated Syphilis



# Neurosyphilis

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- CNS invasion occurs early in infection
- Invasion is independent of concurrent HIV infection

# Neurosypphilis

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## Early

- Asymptomatic (abnormal CSF findings)
- Meningeal (may include ocular and cranial nerve involvement)
- Meningovascular

## Late

- Paresis (brain parenchyma)
- Tabes dorsalis (posterior column)
  - Ataxia, Lightning pains, optic nerve degeneration, Charcot's joints

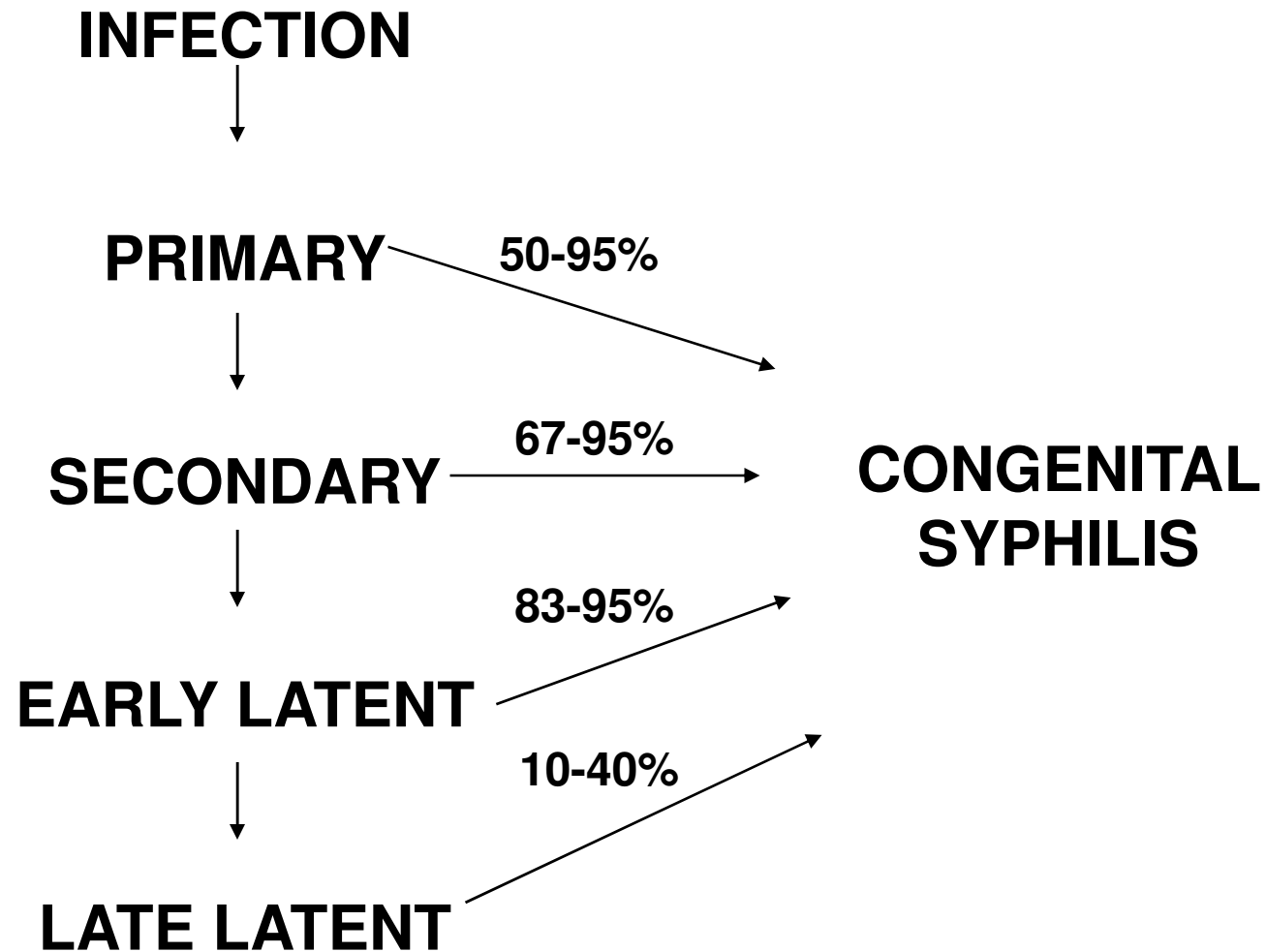
# Congenital Syphilis

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- Transplacental infection can occur
  - Any time during gestation
  - Any stage of syphilis
- Results in spontaneous abortion, stillbirth, infant with active or latent syphilis
- Adequate treatment of pregnant women during 1<sup>st</sup> or 2<sup>nd</sup> trimester is effective for fetus

# Congenital Syphilis by Maternal Stage

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# Manifestations of Congenital Syphilis

- Early:
  - ≤ 2 year
  - Cutaneous lesions
  - Mucous patches
  - Snuffles
  - Hepatosplenomegaly
  - Bone involvement
- Late:
  - > 2 years (often adolescent)
  - Interstitial keratitis
  - 8<sup>th</sup> nerve deafness
  - Bone involvement
  - Hutchinson's incisors, mulberry molars

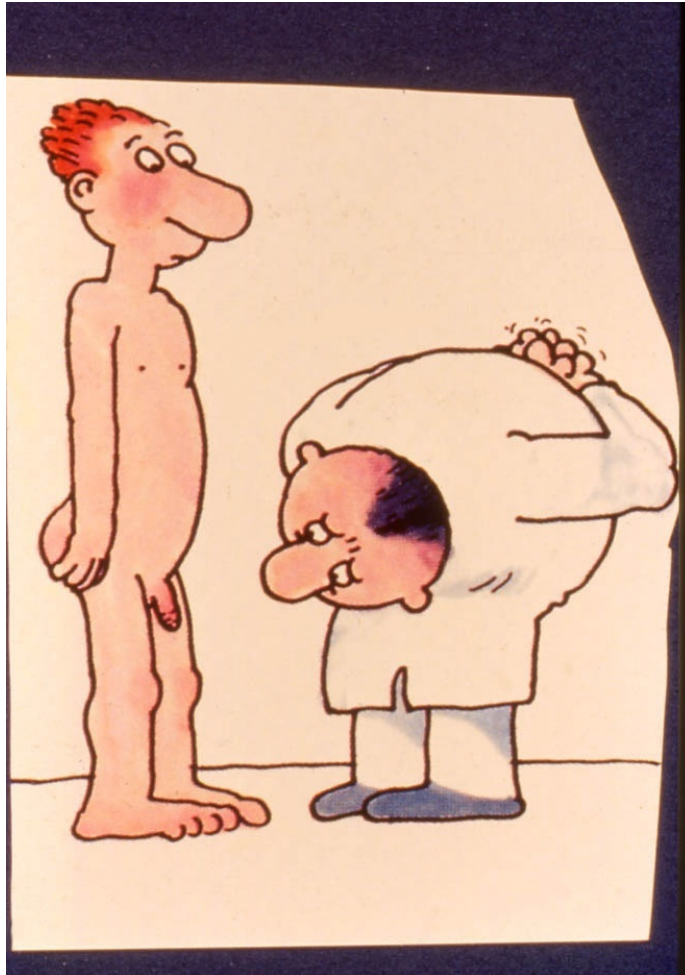


# Syphilis: Diagnosis

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- Clinical manifestations
- Identification of *Treponema pallidum*
- Serological testing

# Clinical Diagnosis



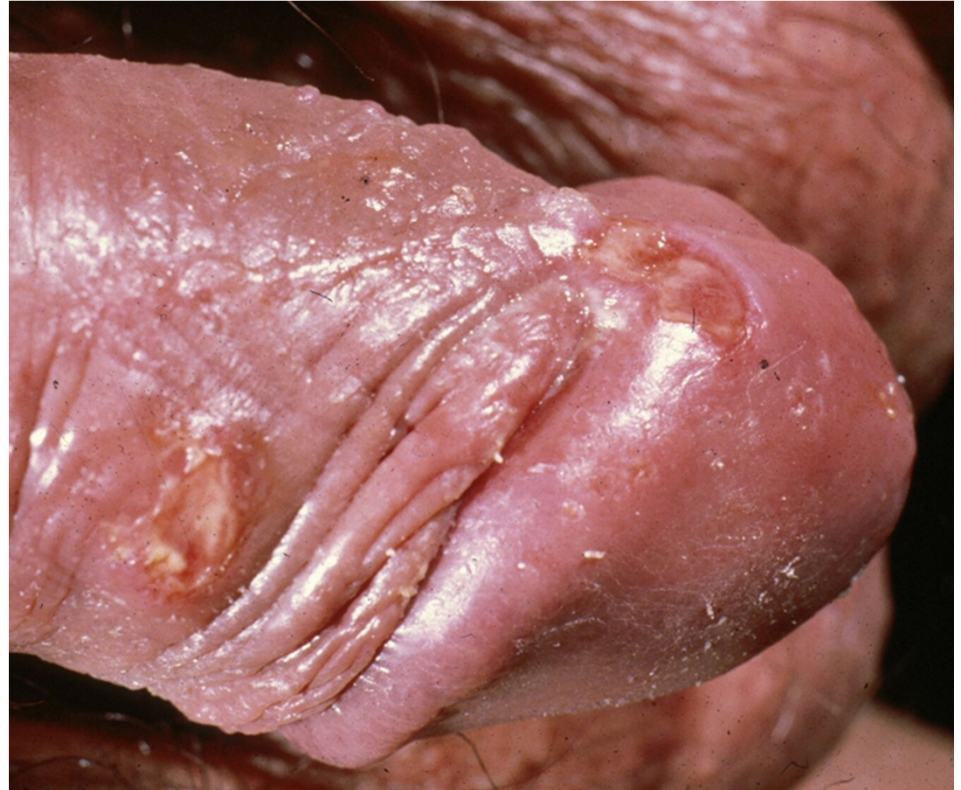
?

# Other Causes of Genital Ulceration

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Herpes



Chancroid



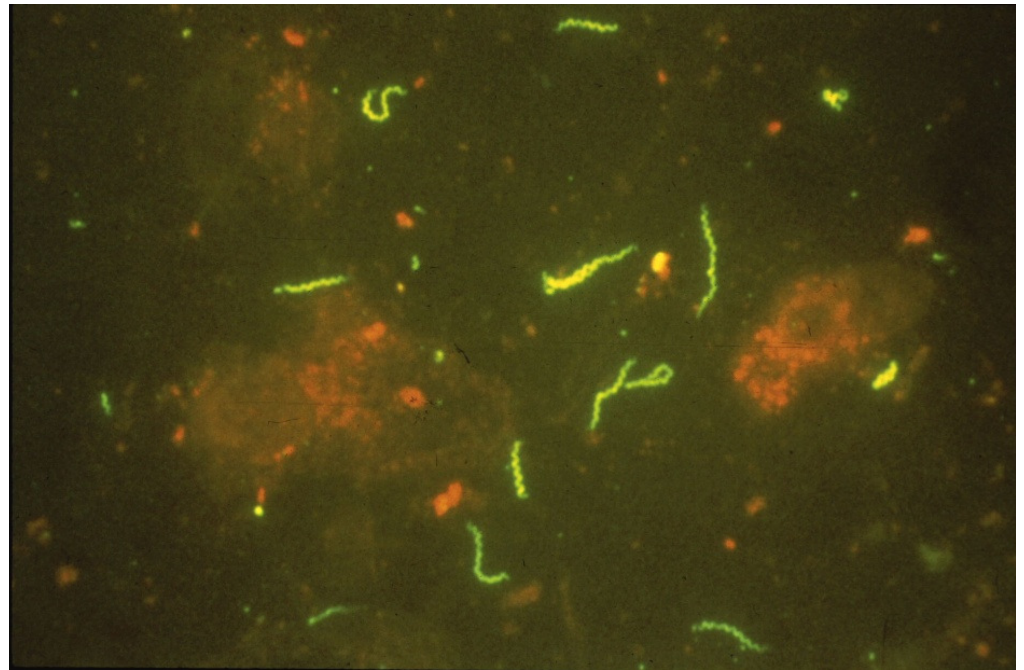
# What is this?



# Direct Detection of *T. pallidum*

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- Darkfield microscopy
- IF staining
- PCR



- None of these is widely available

# Serological Testing for Syphilis

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Nontreponemal



RPR, VDRL

Treponemal



TPPA, EIA/CIA

FTA-Abs

# Syphilis Serology: Nontreponemal Tests

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- RPR – Rapid Plasma Reagin
- VDRL – Venereal Diseases Research Laboratory

Used for screening, quantitation

Detects antibody to a cardiolipin antigen –  
may be falsely positive



# Syphilis Serology: BFP Reactions

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- Acute
  - Recent viral illness, immunization
  - Drug use
  - Pregnancy?
- Chronic
  - Autoimmune condition (SLE, RA)
  - Hypergammaglobulinemia
  - Drug use
  - Aging

# Syphilis Serology: Treponemal Tests

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- TPPA: Particle agglutination
- FTA-ABS: Fluorescent Treponemal Antibody Adsorbed
- Enzyme/chemiluminescence Immunoassays (EIA/CIA)

Used to confirm positive VDRL or RPR

May remain positive after therapy; not useful if history of syphilis

# Sensitivity of Serological Tests in Untreated Syphilis

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## Stage of Disease

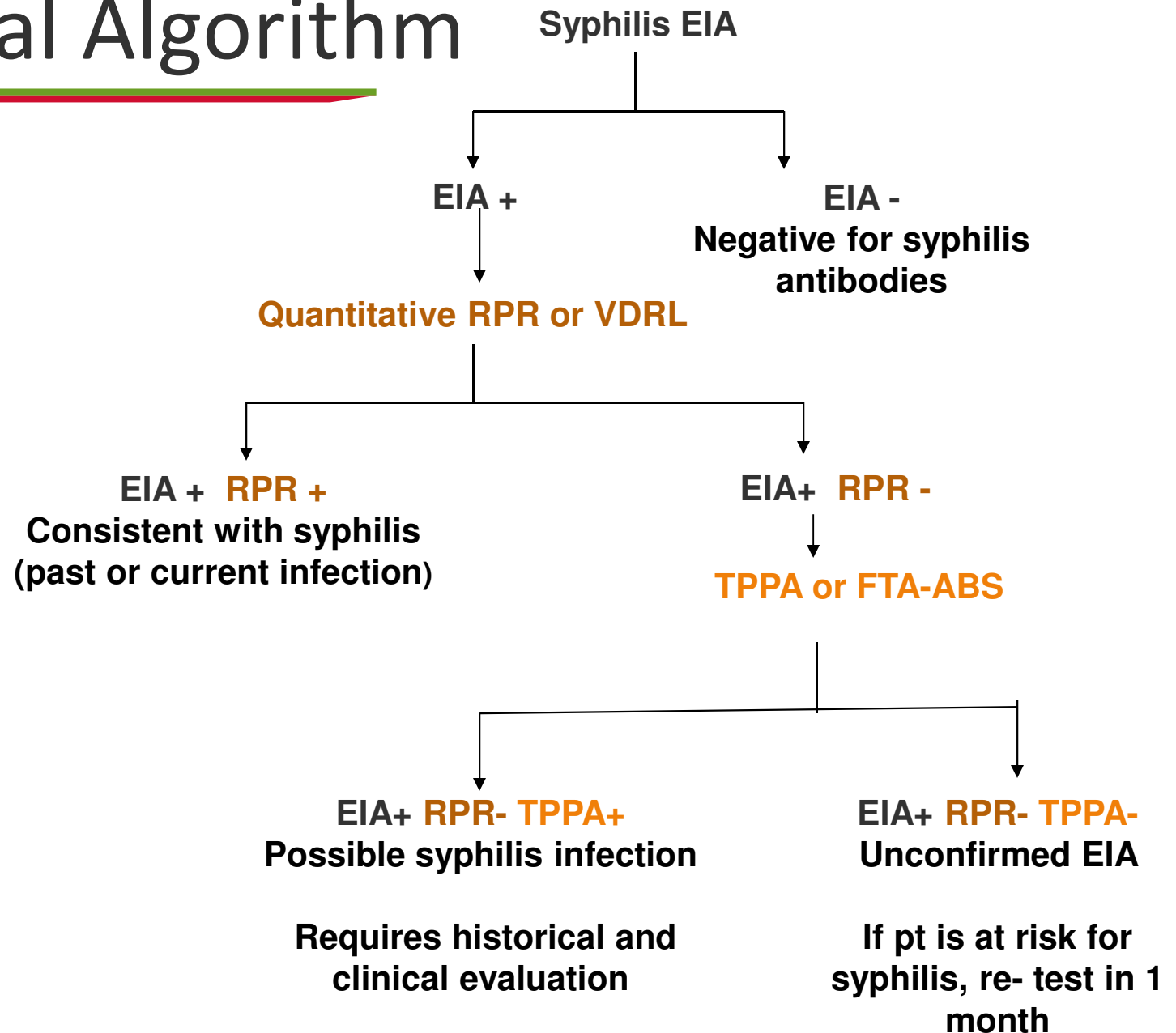
<b>% Positive</b>	<b>Primary</b>	<b>Secondary</b>	<b>Latent</b>
<b>RPR, VDRL</b>	80	100	95
<b>FTA-ABS</b>	84	100	100
<b>TPPA, EIA</b>	89	100	100

# Screening with EIA/CIA Tests

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- Increasingly common in large labs
- Based on 2-3 recombinant antigens
- Many EIA+ RPR- results in low prevalence groups
- How to interpret reactive EIA screening tests?

# Provisional Algorithm



# Syphilis 101

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Lunch and Learn, 12/16/2015

Julie Dombrowski, MD, MPH

Assistant Professor of Medicine, U. of Washington

Medical Director, Public Health – Seattle & King County STD Clinic



UNIVERSITY OF WASHINGTON  
STD Prevention  
Training Center



# Overview

- Treatment and post-treatment follow-up
- Relationship between syphilis and HIV
- Syphilis in pregnant women
- Management of sexual partners

# Treatment and Post-Treatment Follow-Up

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# Case 1

- You are seeing a 27 year-old man who complains of feeling fatigued. You notice a rash on his hands, which he attributes to his job as a dishwasher. He has had 3 male sex partners in the past year and says he uses condoms “pretty much always”.

Do you:

- A) Send a syphilis serology test and counsel him to abstain from sex until the results are back
- B) Treat him with a one-time dose of benzathine penicillin G (B-PCN)
- C) Treat him with 3 weeks of B-PCN
- D) Treatment depends on his HIV status



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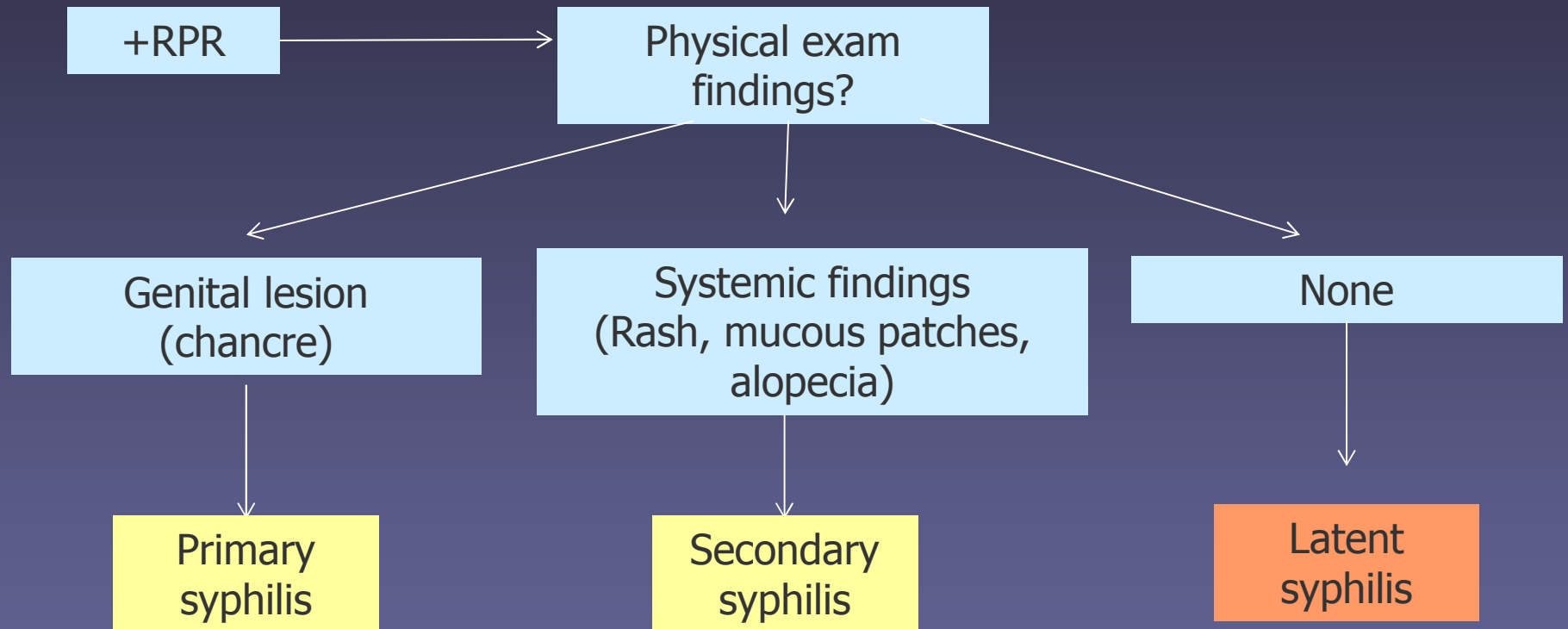
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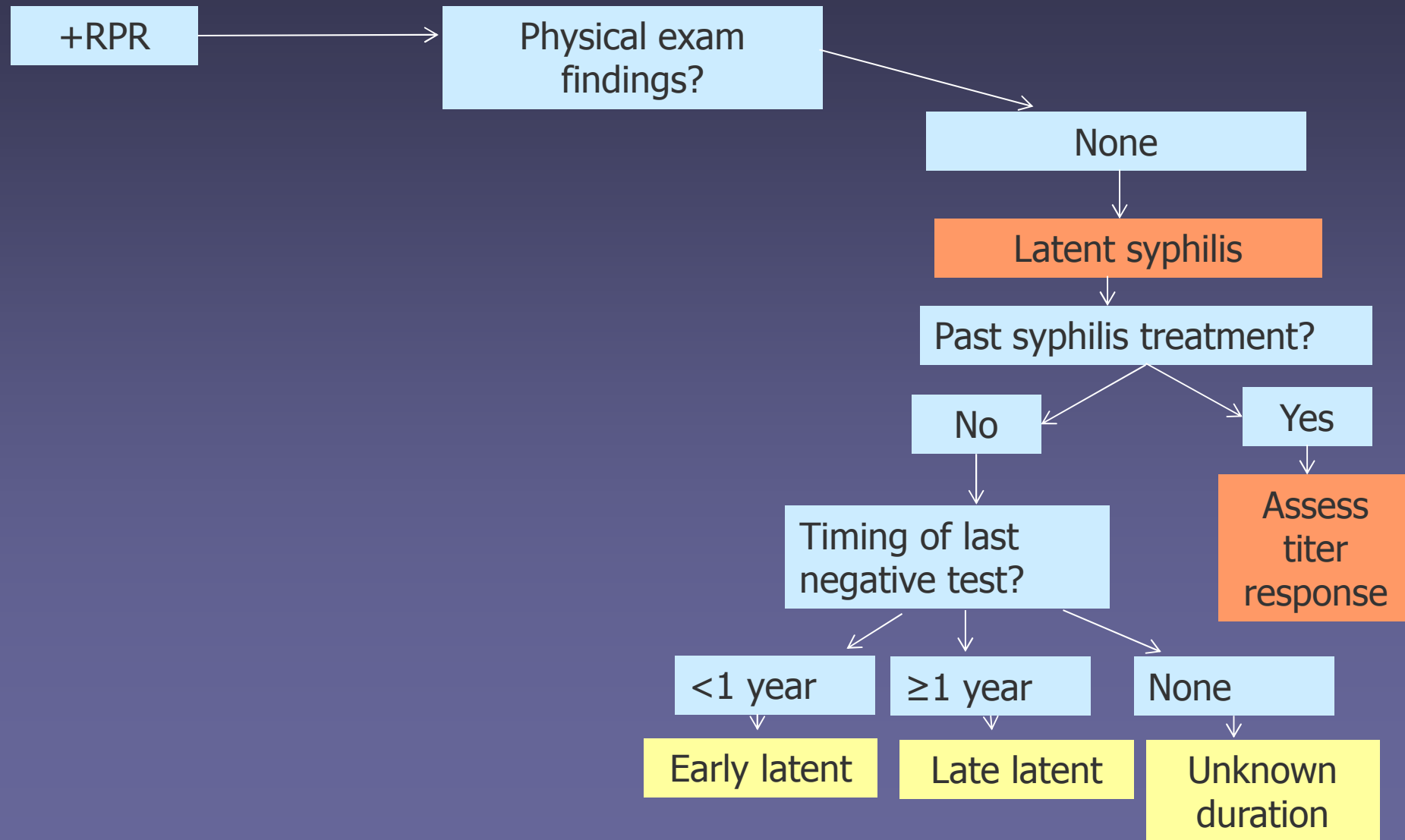
# Staging

- Crucial for treatment & partner notification
  - For treatment
    - Early – one time treatment
    - Late – weekly shots x 3
    - Neuro (with early or late) – intensive 10-14 day treatment
  - For partner notification
    - Longer windows for later disease stage
- Requires history of syphilis testing & treatment, exposure & symptoms, physical exam

# Staging Simplified



# Staging: No Symptoms



# Staging of Latent Syphilis

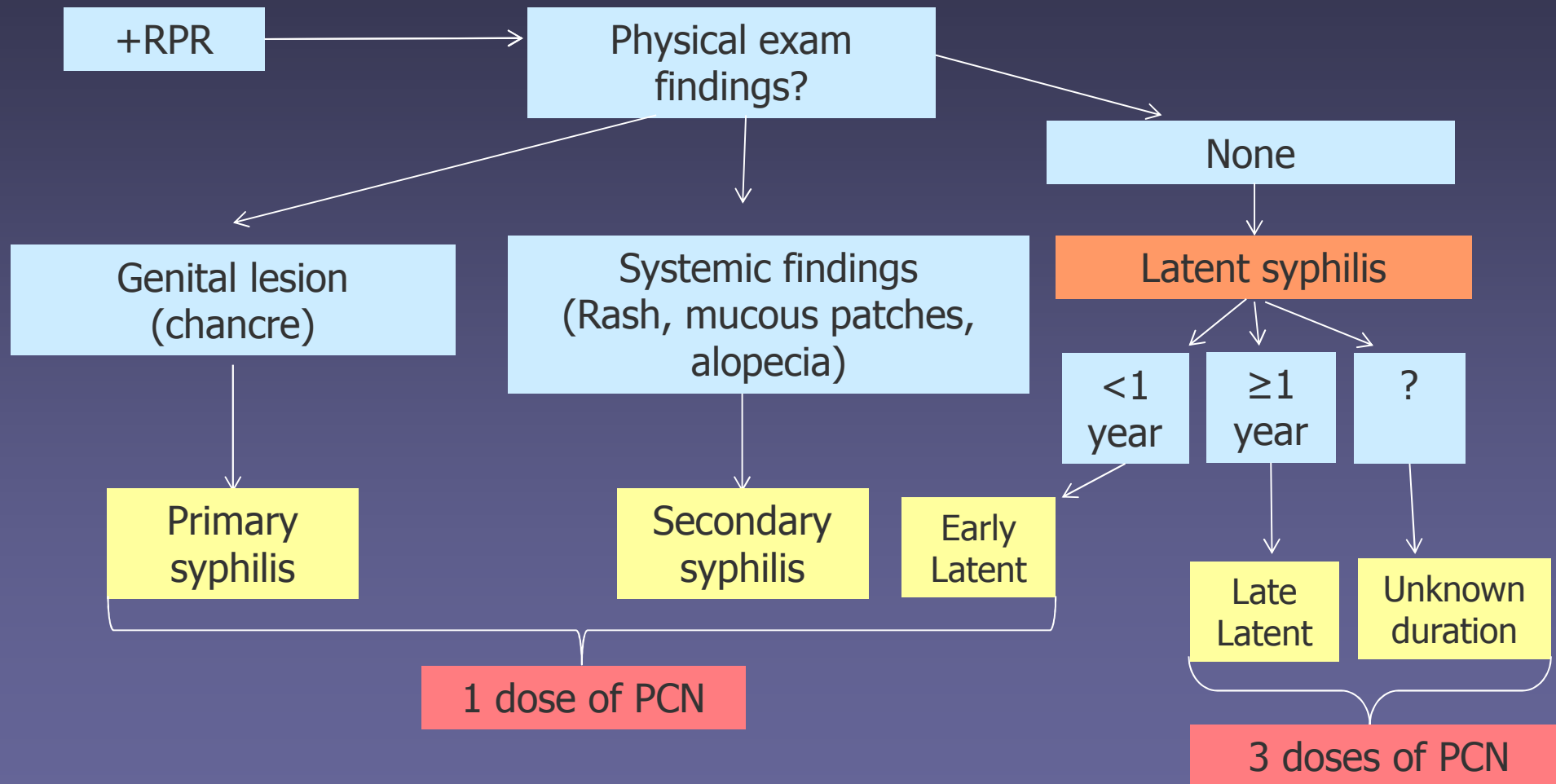
## Early Latent (infected less than one year)

- Negative syphilis serology in past year
- Known contact to an early case of syphilis
- Good history of typical signs/symptoms
- 4-fold increase in titers in past year

## Late Latent (infected > 1 year or unknown duration)

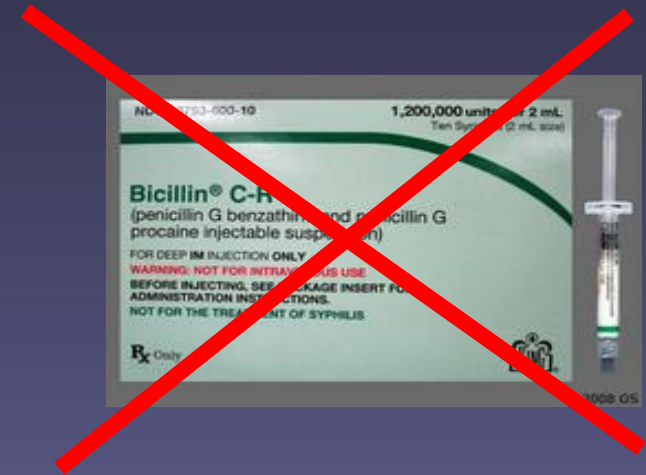
- No syphilis serology in past year
- No contact to syphilis case or history of signs/symptoms in past year

# Treatment Simplified

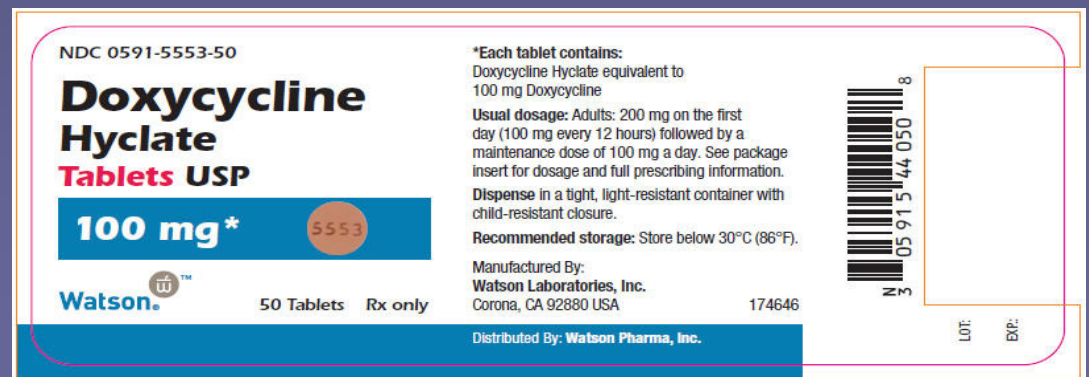


# Treatment Summary

Benzathine penicillin  
2.4 million units IM  
(1 dose for early,  
3 doses for late/unknown)



Penicillin allergy:  
Doxycycline  
100mg po BID  
(2 week for early,  
4 weeks for late/unknown)





# Case 1

( 27 year-old MSM with palmar rash )

■ What else do you need to do today?

- Assess for symptoms of neurosyphilis
- Warn him about the Jarish-Herxheimer reaction
- TEST FOR HIV
- Report the case
- Counsel patient to refer partners for evaluation



# Neurosypphilis

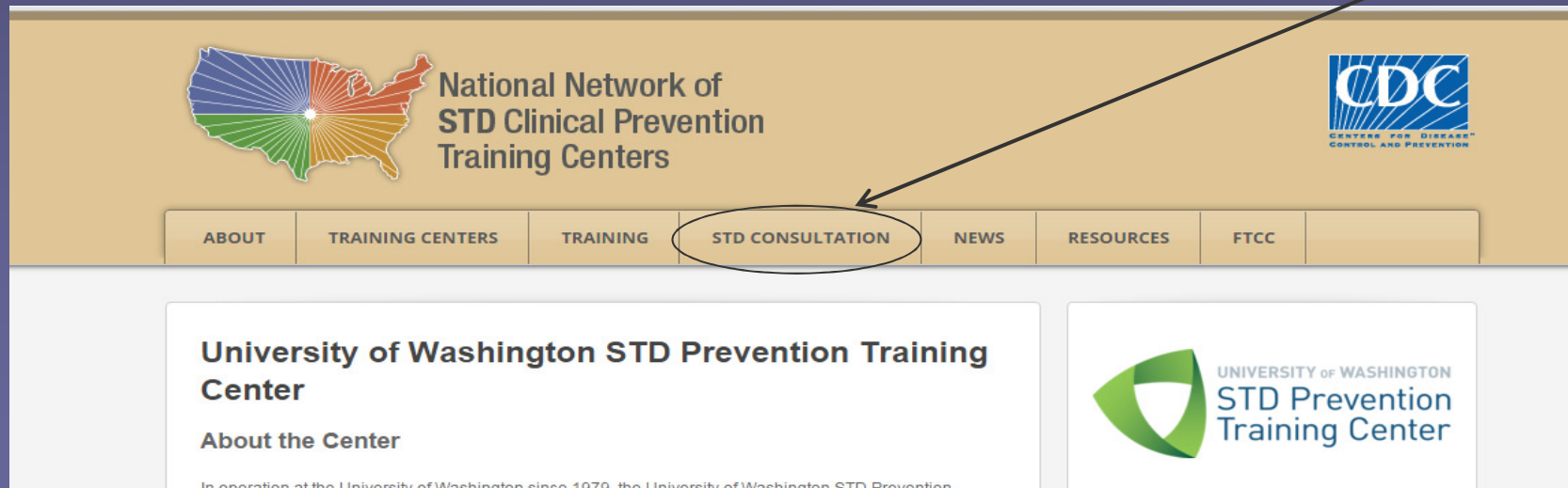
- Invasion of central nervous system by *T. pallidum*
- Untreated, can progress to meningovascular syphilis (stroke), late neurologic complications
- Ocular syphilis can lead to permanent blindness
- Otosyphilis can lead to permanent hearing loss
- Imperative to screen everyone diagnosed with syphilis at any stage

# Neurosyphilis – Screening Questions

- Changes in vision? (blurry vision)
- Changes in hearing?
- Tinnitus?
- Headaches?

LP  
Opthalmologic &  
Otologic referrals

Consult health  
department and  
Seattle PTC



ry loss,

# Jarisch – Herxheimer reaction

- Fever, malaise, nausea, vomiting, chills, exacerbation of rash
- Especially in secondary
- Within 24 hours, resolves in 24 hours
- Supportive care

# Titer follow-up

- Follow titers at 6 and 12 months (our STD Clinic practice is 1, 3, 6, 9, 12 months)
- Failure or reinfection
  - Persistent or recurrent symptoms
  - Sustained 2 titer (4-fold) rise in RPR/VDRL
  - High titer syphilis (RPR  $\geq 1:32$ ) that does not decline 4-fold over 6-12 months (1<sup>o</sup> or 2<sup>o</sup>) or 12-24 months (latent syphilis)
- Eventually to NR in most people.
- Serofast reaction: low titer long time (maybe for life)
- Must follow same test: RPR or VDRL
- RPRs often 1-2 fold higher than VDRL

# Rescreening

- Like other bacterial STDs, reinfection rates are substantial
- Public Health –Seattle & King County recommendations
  - High-risk MSM should test q 3 months
    - Bacterial STD in past year
    - Methamphetamine or popper use
    - Unprotected anal intercourse with HIV+ or unknown partners
    - $\geq 10$  sex partners in past year
  - All other sexually active MSM should test annually

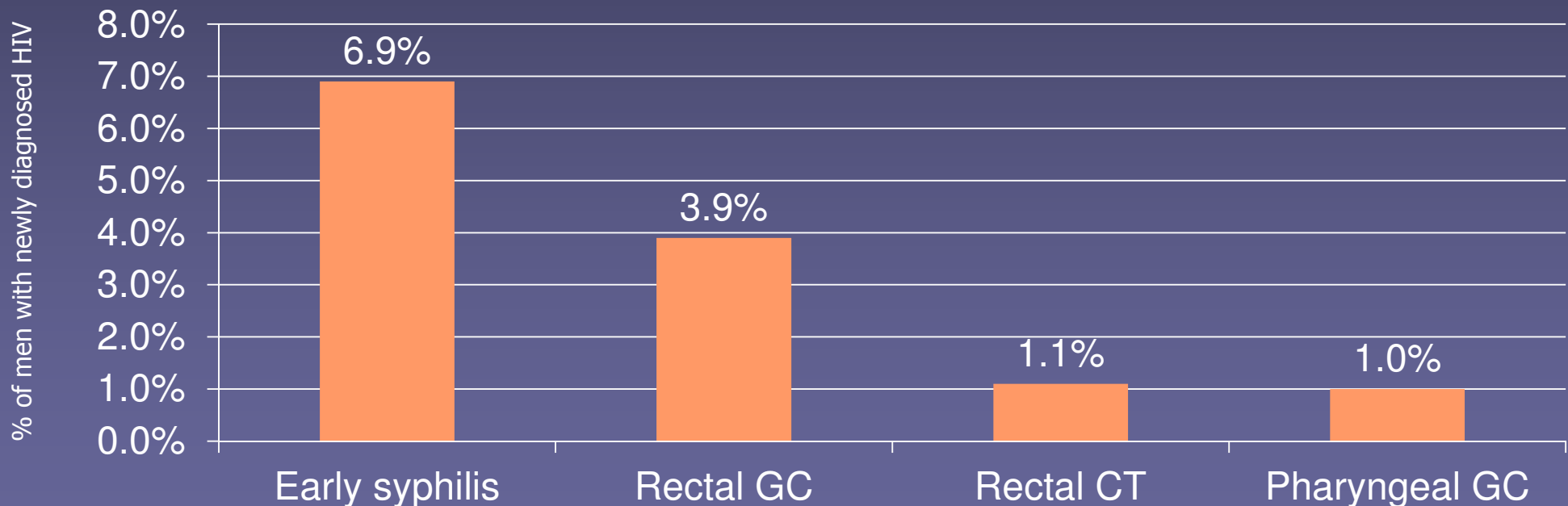
# Syphilis and HIV

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# HIV Testing

- Undiagnosed HIV is common among MSM with syphilis
- All persons with syphilis should be tested for HIV

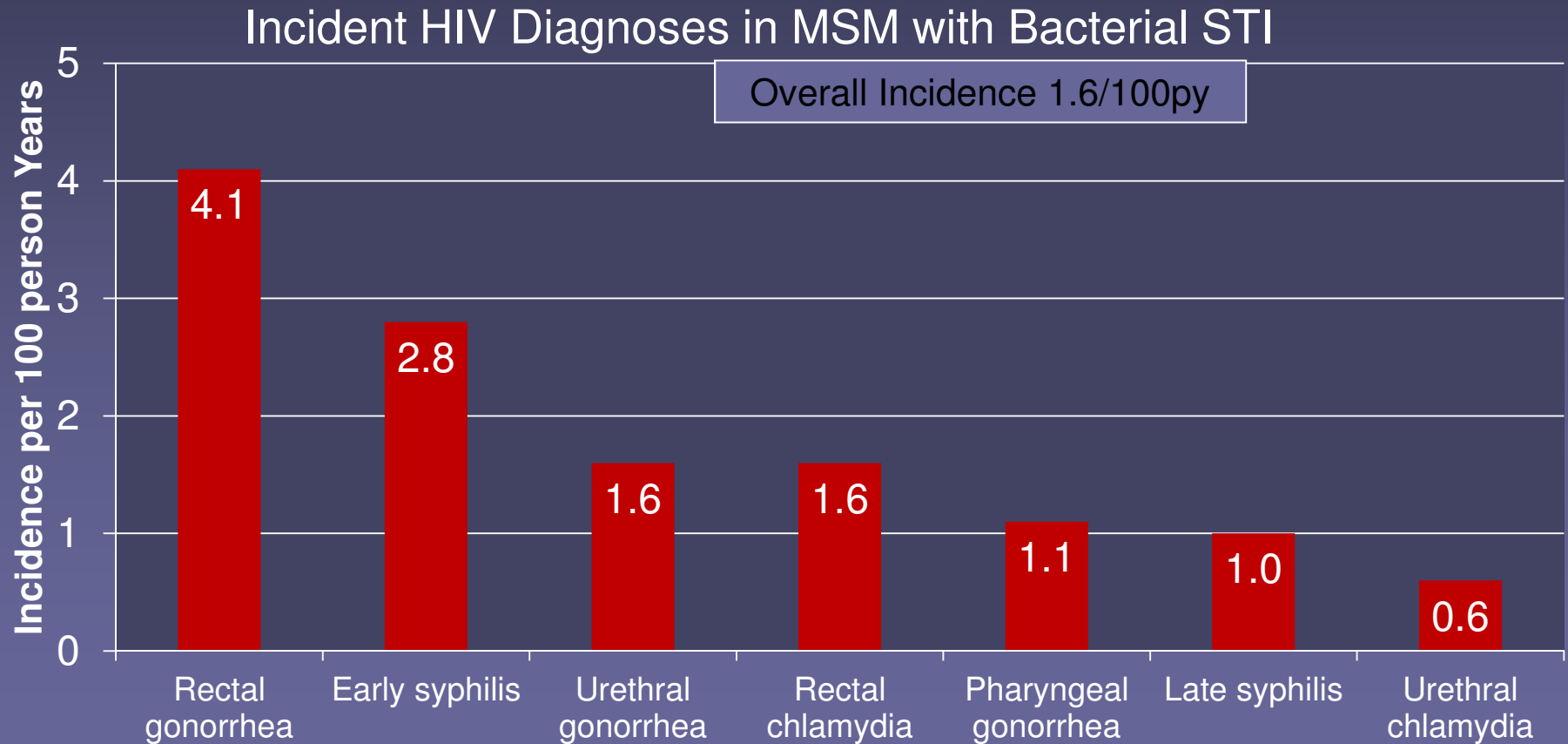
## Newly Diagnosed HIV among MSM with Bacterial STDs in Washington State, 5/2012 – 8/2014





# HIV Pre-Exposure Prophylaxis (PrEP)

- HIV incidence in MSM with bacterial STI varies by pathogen and site of infection



Katz, D (unpublished)

# Syphilis in Pregnant Women

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# Case 3

You screened a 26 year-old woman from Guatemala for syphilis at her first prenatal visit (G0P1). She and her husband have been monogamous and married for 3 years. Her test results are:

- *T. pallidum* EIA: POSITIVE
- Rapid plasma reagin (RPR): NEGATIVE
- *T. pallidum* particle agglutination assay (TPPA): POSITIVE

What do you do?

- A) Tell patient she has syphilis; treat her for early latent syphilis (1 shot B-PCN)
- B) Tell patient she might have syphilis; treat her for late latent syphilis (3 shots B-PCN)
- C) Tell patient she does not have syphilis. This is a false positive test result.

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# Congenital Syphilis – U.S.

- A case of congenital syphilis is a sentinel event
  - Failure of healthcare and public health system
- Elimination is one of the top four strategic priorities of CDC STD Control Branch
- Achievable goal?
  - 458 cases in 2014
    - Increase from 334
    - Biggest rate increase in Western US

# Syphilis & Pregnancy

- Screening
- All women should be screened early in pregnancy (usually first prenatal visit)
- “High risk”
  - Twice during third trimester (usually 28-32 weeks)
- Any woman who delivers a stillborn infant after 20 weeks

# Syphilis & Pregnancy

- Positive screen + history of treatment
  - Was appropriate treatment documented?
  - Was response adequate?
    - Non-treponemal titers at 6, 12, and 24 months
    - Decline  $\geq$  fourfold (i.e.  $\geq 2$  dilutions) within 12-24 months of therapy
    - Serofast reaction = persistent positivity for years to lifelong



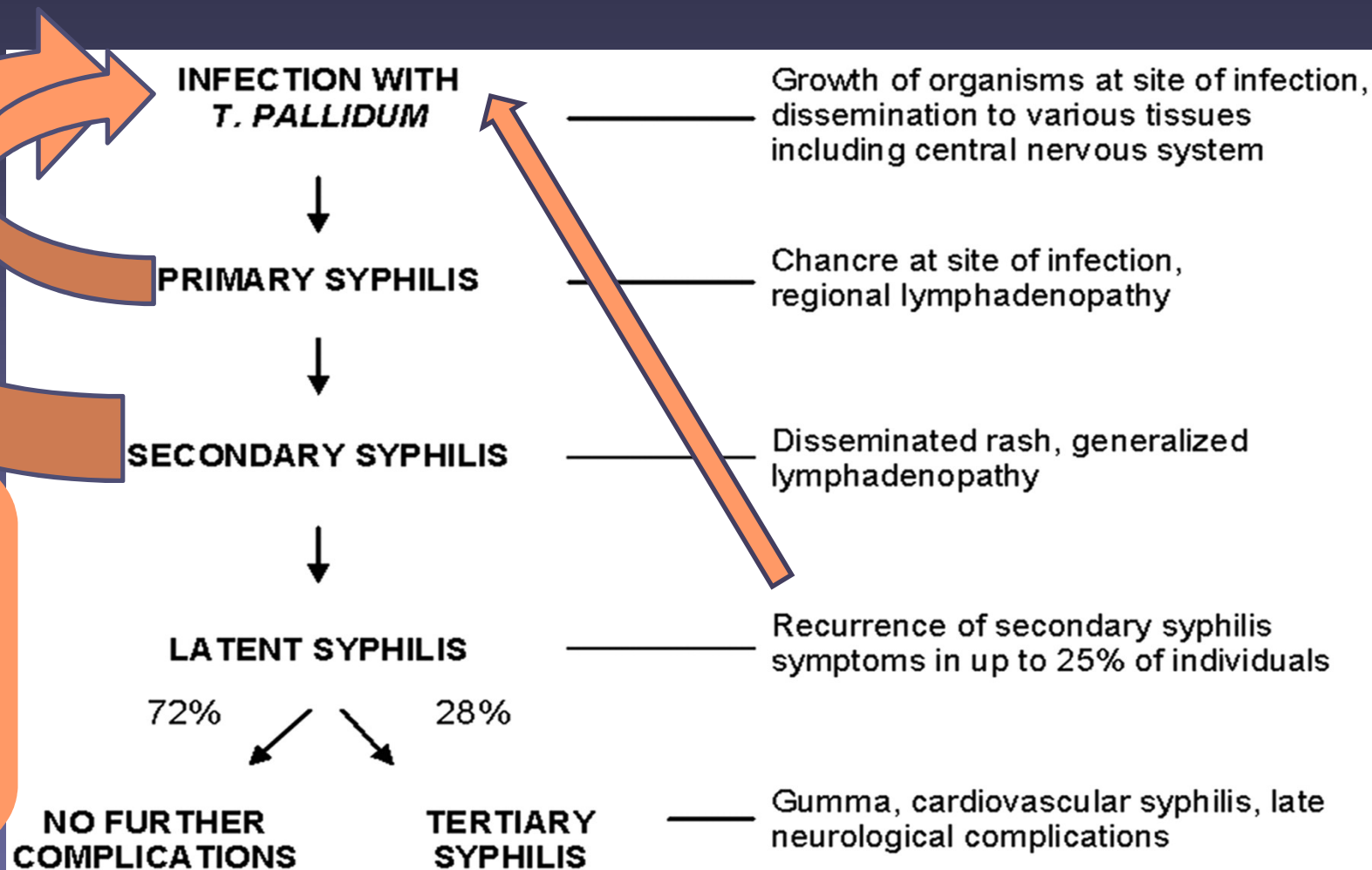
# Syphilis & Pregnancy

- If positive screen and no history of treatment
  - Penicillin effective for preventing transmission to fetus and treating fetal infection
  - Treat with penicillin appropriate for stage of infection
    - Primary, secondary, early latent: benzathine penicillin G 2.4 million units x 1
    - Late latent or unknown duration: benzathine penicillin G 2.4 million units weekly x 3 weeks
    - Assess for neurologic symptoms at any stage of infection
  - Reassess titers at 28-32 weeks and delivery
  - If RPR still reactive at delivery: check RPR and examine child for e/o congenital syphilis
    - Hydrops fetalis, jaundice, hepatosplenomegaly, rhinitis, rash, pseudoparalysis of an extremity)

# Partner management

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# Transmission



Risk: ~30% per sex act

(compared to 0.07-2% per sex anal sex act for HIV\*)

# Partner management

- Diagnosing providers required to complete case report
- Labs also report results directly to public health
- Disease intervention specialists call all persons diagnosed with syphilis for interview and assistance with partner notification
  - You can help with this process by preparing your patients for this call!
- All contacts should be treated, regardless of test results due to the risk of incubating (RPR and EIA negative) syphilis

# Syphilis Take Home Points

- Prompt diagnosis and treatment require a high level of suspicion
- All persons with syphilis should be tested for HIV
- MSM who acquire syphilis should screen for STD/HIV every 3 months for at least a year
- Seattle PTC clinicians are happy to help you with diagnostic and treatment quandries

# Thank you!

- [jdombrow@uw.edu](mailto:jdombrow@uw.edu)
- CDC STD Treatment Guidelines
  - <http://www.cdc.gov/std/tg2015/>
- National Network of Clinical Prevention Training Centers
  - <http://nnptc.org/training-centers/seattle/>